ELEVATED FREQUENCIES OF HYPERHAPLOID SPERM WERE DETECTED IN A MAN WITH A HISTORY OF MULTIPLE ANEUPLOID PREGNANCIES.

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The goal of this research is to determine the heritable risk associated with elevations in the proportion of hyperhaploid human sperm. A case family presented with a history of four aneuploid pregnancies: two with autosomal trisomies (47,+22 and 47,+15) which were non-viable and two children with sex chromosomal aneuploidies (47, XYY and Klinefelter syndrome, 47,XXY). The father consumed ~1/2 pack of cigarettes and 1 alcoholic drink per day. He had no notable occupational or environmental exposures. Paternal origin of extra X chromosome in the boy with Klinefelter syndrome was confirmed by DNA analyses of blood using polymorphic X-linked microsatellite markers. The inheritance pattern was established by ≥2 informative loci using PCR products analyzed on an automatic DNA sequencer. Multi-probe sperm FISH was employed to determine the proportion of sperm with aneuploidies involving chromosomes 21, X, and Y. Sperm of four healthy men were scored blinded with the same FISH assay (≥10,000 sperm per man) and served as a reference group; one donor was scored concurrently and three prior. Sperm aneuploidy frequencies did not differ among the reference men. In comparison, the case father showed highly elevated frequencies of hyper-haploid sperm; XY (~6 fold, $p < 0.001$), 21-21 (~6 fold, $p< 0.001$), XX and YY (~2 fold, $p<0.02$). These findings suggest that elevated proportions of aneuploid sperm may be associated with an increased risk of fathering an aneuploid offspring. These findings are also relevant for future studies of heritable risk for men with elevations in sperm aneuploidy after exposures to therapeutic or environmental agents. [Supported by NIEHS Superfund grant P4ZES04705 to Berkeley and partially performed under the auspices of the U.S. DOE by the Lawrence Livermore National Laboratory under contract W-7405-ENG-48]